REMARKS

Claims 1-10 are pending and stand rejected. Applicants gratefully acknowledge the withdrawal of the prior art rejections of the pending claims. The specification has been amended in accordance with the various requests made in the outstanding Office Action. Claim 2 was amended to specify the nature of the solutes filtered. Support for this amended is found at page 35, lines 23-26. No new matter has been added and entry of the amendment is respectfully requested.

Amendments to the Specification

The U.S. Patent and Trademark Office ("Office") requested that Applicants change the title of the present application to delete the reference to compositions; this amendment has been made.

The Office requested that Applicants update the claim of priority in the specification. Applicants have amended the first paragraph of the specification to recite U.S. Patent No. 6,352,975, which issued from Application No. 09/392,932.

Finally, the Office objected to the specification because of an incomplete sentence at page 23, line 10. Applicants have deleted this sentence fragment.

Applicants' failure to address these matters in the previous response was an oversight, which has now been corrected.

The pending claims are fully supported by an enabling disclosure

Claims 1-10 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement. The test for enablement is whether the full scope of the claimed invention can be practiced without undue experimentation. *In re Wright*, 999 F.2d 1557, 1561 (Fed. Cir. 1993).Moreover, in *Regents of University of California v. Eli Lilly & Co.*, the Federal Circuit held

that enablement of a genus under § 112, ¶ 1, may be accomplished by showing the enablement of a representative number of species within that genus. 119 F.3d 1559 (Fed. Cir. 1997). Enablement "is not precluded even if some experimentation is necessary, although the amount of experimentation needed must not be unduly extensive." *See Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367 (Fed. Cir. 1986). Applicants respectfully submit that one of ordinary skill in the art would be able to practice the full scope of the pending claims without undue experimentation.

The Office has alleged that the pending claims lack enablement because the claims read on treating hypertension generally, without regard to the etiology of the condition. Applicants agree with this interpretation of the claims. The methods recited in the pending claims are directed to treating hypertension, regardless of etiology.

In the Action, the Office classifies hypertension in two different categories, essential hypertension and hypertension with a known causality, such as salt-dependent hypertension. The Office readily admits that the present disclosure enables the treatment of salt-dependent hypertension. In fact, the Office issued U.S. Patent No. 6,352,975 on just such a method. The Office, however, alleges that it would require undue experimentation to for one of ordinary skill in the art to treat other hypertensive states not related to salt intake.

Applicants have demonstrated that the claimed method is effect to treat both salt-dependent hypertension as well as a salt-independent hypertension model. Working examples present in the specification demonstrate that the claimed method is effective to reduce hypertension in a salt-dependent model. The last response filed by Applicants, provided data in the form of a Rule 132 declaration by Dr. Schreiner, which showed that the claimed method also functioned in a salt-

independent hypertension model. Applicants respectfully submit that these showings more than adequately illustrate that the specification of the present application more than adequately enables the claimed treatment method. As such, the present rejection should be withdrawn.

The Rule 132 declaration did not persuade the Office, which issued the outstanding final Office Action, maintaining the enablement rejection of the pending claims. The final Action suggested that the accepted animal model for essential hypertension is the spontaneous hypertensive rate (SHR) model. Applicants respectfully disagree with the Office's assertion that the experimental evidence provided was not sufficient to demonstrate that the present claims are fully enabled by the specification. Nevertheless, solely to advance prosecution of the present case, Applicants provide for the Office's benefit, a copy of Yang, R., *et al.*, "Exaggerated hypotensive effect of vascular endothelial growth factor in spontaneously hypertensive rats," Hypertension. 2002 Mar 1;39(3):815-20.

The Yang paper reports the hypotensive effects of VEGF administration to spontaneously hypertensive rats (SHR). Yang *et al.* administered VEGF to SHR and normotensive Wistar-Kyoto rats (WKY) and observed the effect of the treatment on *inter alia*, mean arterial blood pressure (MAP). As dramatically depicted in Figure 1A of the paper, SHR rats showed a marked decrease in MAP as compared to the normotensive WKY rats. Thus, the work reported in this paper clearly demonstrates that the administration of VEGF is effective to lower blood pressure in both salt-dependent and salt-independent models.

The experimental data provided in the specification, in the Rule 132 declaration of Schreiner, and the Yang reference all clearly demonstrate that the claimed method of treating

hypertension is fully enabled. Accordingly, Applicants request that the present rejection be withdrawn and the case be passed to issuance.

Claims 2-4 were also rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement. Specifically, the Office alleged that the nature of a solute was not sufficiently defined and that there was no evidence of record that excretion of solutes was improved by VEGF administration.

In response, Applicants have amended claim 2 to clarify the subject matter regarded as the invention. By specifying that the solutes filtered are renal solutes, one of ordinary skill in the art would readily recognize that the solutes that VEGF administration acts upon are those that are normally filtered by the kidney. Such solutes include urea, creatinine, uric acid, urates, sodium ions, potassium ions, chloride ions, and excess hydrogen ions. Because the identity of renal solutes is well known to those of ordinary skill in the art, there is no need for Applicants to disclose these specifically in the specification. Moreover, the specification clearly contemplates the use of VEGF to increase renal filtration, for example, by increasing glomerular permeability (specification, page 9, lines 17-29). As such, Applicants submit that the subject matter of claims 2-4 are fully enabled.

CONCLUSION

Applicants have endeavored to address all of the Examiner's concerns as expressed in the outstanding Office Action. Accordingly, amendments to the claims, the reasons therefor, and arguments in support of the patentability of the pending claim set are presented above. Any claim amendments which are not specifically discussed in the above remarks are made in order to improve the clarity of claim language, to correct grammatical mistakes or ambiguities, and to otherwise improve the capacity of the claims to particularly and distinctly point out the invention to those of skill in the art. In light of the above amendments and remarks, reconsideration and withdrawal of the outstanding rejections is specifically requested. If the Examiner finds any remaining impediment to the prompt allowance of these claims that could be clarified with a telephone conference, the Examiner is respectfully requested to initiate the same with the undersigned.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicants petition for any required relief including extensions of time and authorize the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket No. 219002030901.

Respectfully submitted,

Dated: August 10, 2004 By: _____

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